MARKED VERSION OF PAGE 32 OF THE SPECIFICATION

breast tissue and breast cancer. Thus, the mammary gland disorder can be cystic breast disease. The botulinum toxin can be locally administered by direct injection of the botulinum toxin into the mammary gland.

A more detailed embodiment of the present invention is a method for treating a mammary gland disorder by local administration of between about 10^{-3} U/kg and about 2000 U/kg of a botulinum toxin type A to a mammary gland of a human patient, thereby a mammary gland disorder.

Our invention also encompasses a method for treating a mammary gland disorder by local administration of a botulinum toxin to a mammary gland or to the vicinity of a precancerous breast tissue, thereby causing a reduction in the size and/or activity of a ~~hyperplastic~~ hyperplasic, hypertonic or neoplastic mammary gland tissue. This method can reduce the diameter of the ~~hyperplastic~~ hyperplasic, hypertonic or neoplastic mammary gland tissue by between about 20% and about 100%, subsequent to the local administration of the botulinum toxin.

Thus a method for treating a mammary gland disorder as disclosed herein can comprise the step of local administration of a therapeutic amount of a botulinum toxin to a ~~hyperplastic~~ hyperplasic, hypertonic or neoplastic mammary gland tissue, thereby causing a reduction in the diameter of the ~~hyperplastic~~ hyperplasic, hypertonic or neoplastic mammary gland tissue of between about 20% and about 100%.

Additionally, the present invention encompasses a method for preventing development of a mammary gland neoplasm, the method comprising the step of local administration of a botulinum toxin to a hyperplasic or hypertonic mammary gland tissue, thereby reducing a secretion from the hyperplasic or hypertonic

mammary gland tissue and preventing the hyperplasic or hypertonic mammary gland tissue from developing into a neoplasm. In this method the botulinum toxin is administered in an amount of between about 10^{-3} U/kg and about 2,000

MARKED VERSION OF PAGE 34 OF THE SPECIFICATION

method comprising the step of local administration of between about 10^{-3} U/kg and about 2000 U/kg of a botulinum toxin type A to a ~~hyperplastic~~ hyperplasic, metaplasic or atypical breast tissue (such as an apocrine cell lined cyst) of a human patient, wherein the breast tissue comprises a substrate for the botulinum toxin selected from the group of vesicle membrane docking proteins consisting of a 25 kiloDalton synaptosomal associated protein (SNAP-25), synaptobrevin and syntaxin, and wherein the botulinum toxin acts upon the substrate to reduce a secretion from the afflicted breast tissue.

The present invention includes within its scope a method for treating a neoplasm by local administration of between about 10^{-3} U/kg and about 2000 U/kg of a botulinum toxin to the neoplasm, thereby treating the neoplasm by either reducing the size of the neoplasm and/or by reducing a secretion from the neoplasm.

A method according to the present invention can be carried out by direct injection of a botulinum toxin into the body of a neoplasm or by implantation of a botulinum toxin implant into or onto the body of the neoplasm. A method within the scope of the present invention can be practiced to locally administer between about 10^{-3} U/kg and about 2000 U/kg of a botulinum toxin to a neoplasm. U/kg means units of a botulinum toxin per kilogram of total patient weight. The botulinum toxin can be one of the botulinum toxin types A, B, C_1, D, E, F and G, and is preferably a botulinum toxin type A because of the known clinical efficacy of botulinum toxin type A for a number of indications and because of its ready availability.

Preferably, the botulinum toxin is administered in an amount of between about 1 U and about 40,000 U (total units, not per kg of patient weight). At the higher dose ranges the amount of botulinum toxin administered (i.e. 40,000

units) can be administered in the form of a controlled release delivery system (i.e. an implant), whereby fractional amounts of the botulinum toxin depot (i.e.

MARKED VERSION OF PAGE 50 OF THE SPECIFICATION

If the pancreatic duct is not accessible or does not decompress, a percutaneous needle, imaging guided (i.e. by ultrasound or computed tomography) can also be used for transabdominal injection of a neurotoxin directly into pancreatic tissue. Thus, percutaneous needle aspiration for pancreatic biopsy is a known technique and aspiration can be reversed to accomplish the desired toxin injection. Thus, an insulinoma or hypertonic or hyperplasic pancreatic tissue can be treated by local administration of from 1 500 units of a botulinum toxin to the pancreatic target tissue. Neoplastic or ~~hyperplastic~~ hyperplasic lung, intestinal and ovarian target tissue can likewise be treated,

(2) Pituitary

Stereotactic procedures can be used for precise intracranial administration of neurotoxin in aqueous form or as an implant to treat a hyperplasic or hypothalamus or pituitary target tissue. A cranial neuroblastoma is also treated in this manner. Thus, intracranial administration of a botulinum toxin can be carried out as follows.

A preliminary MRI scan of the patient can be carried out to obtain the length of the anterior commissure-posterior commissure line and its orientation to external bony landmarks. The base of the frame can then be aligned to the plane of the anterior commissure-posterior commissure line. CT guidance is used and can be supplemented with ventriculography. The posterior commissure can be visualized on 2-mm CT slices and used as a reference point.

Physiological corroboration of target tissue localization can be by use of high and low frequency stimulation through a electrode accompanying or incorporated into the long needle syringe used. A thermistor electrode 1.6 mm in diameter with a 2 mm exposed tip can be used (Radionics, Burlington, Massachusetts). With

electrode high frequency stimulation (75 Hz) paraesthetic responses can be elicited in the forearm and hand at 0.5-1.0 V using a Radionics lesion generator